Remarks

Applicants have replaced the sequence listing with a Substitute Sequence Listing to correct a discrepancy regarding the negative numbering of the first 20 residues of SEQ ID NO:2, and to update the format of the sequence listing to comply with the presently pending sequence requirements (37 C.F.R. §§ 1.821 to 1.825). No new matter has been introduced.

Claims 23-38 and 41-48 are pending; the Examiner has indicated that claims 24-37 would be allowable if rewritten in independent form.

I. Amendment of the Sequence Listing

The Examiner has requested clarification of the numbering of the first 20 residues of SEQ ID NO:2, noting that the description of the numbering of such residues in the specification and figures was inconsistent with lack of negative numbers for the leader sequence. *See* Paper No. 21, pages 2-3.

In response, Applicants thank the Examiner for pointing out this clerical error in the sequence listing. Applicants note that while the sequence listing in the priority case numbered the first 20 residues of SEQ ID NO:2 with negative numbers, through a clerical error (and contrary to the description in the specification), such residues were numbered in the original sequence listing in this case without negative numbering. As described above, Applicants have corrected this clerical error in the Substitute Sequence Listing submitted herewith. The corrected numbering of SEQ ID NO:2 is fully supported by the specification as originally filed. In particular, support for the amendment to the sequence listing can be found, *inter alia*, at page 7, lines 6-13; and at page 11, lines 10-11. No new matter has been introduced.

Thus, the numbering of the leader sequence of SEQ ID NO:2 in the sequence listing is now consistent with the description thereof in the specification. Applicants therefore respectfully submit that the Examiner's concerns have been obviated.

II. Priority

The Examiner has alleged that the instant application is not entitled to the benefit of the filing date of U.S. Provisional Application No. 60/052,870. *See* Paper No. 21, page 2. The Examiner further alleges that "the effective filing date of this application is 15 July 1998 and not 16 July 1997." *Id.*

However, the instant application also claims the benefit under 35 U.S.C. § 119(e) of U.S. Provisional Application Nos. 60/055,952, filed August 18, 1997 (*see* Preliminary Amendment dated September 20, 1999), and 60/060,140, filed September 26, 1997 (*see, e.g.,* Official Filing Receipt; Specification at page 1, lines 1-7), yet the Examiner has not addressed these priority claims. Accordingly, Applicants respectfully assert that the Examiner's allegation that "the effective filing date of this application is 15 July 1998" is incorrect and should be withdrawn.

OK

For the Examiner's convenience, Applicants have attached herewith an alignment of SEQ ID NOS:1 and 2 from the instant application and from Application No. 60/060,140.

III. Rejection of Claims 23, 38, and 41-48 Under 35 U.S.C. §112, First Paragraph

The Examiner has maintained the rejection of claims 23, 38, and 41-48 under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the

art that the inventors, at the time the application was filed, had possession of the claimed invention. *See* Paper No. 21, pages 3-4. In particular, the Examiner has rejected claim 23(o) and claims dependent thereon, contending that "[a]lthough Applicants teach a general methodology of how to obtain the claimed mature protein, they do not describe the structure of the mature protein and the skilled artisan would not be able to visualize the structure of said mature [form] solely based on the method of obtaining it." *Id.* at page 4.

Applicants respectfully disagree and traverse this rejection. In particular, this rejection should be withdrawn because (1) the specification and claims 23(o) and 38 relate to polynucleotides encoding the mature forms of the IL-20 polypeptide encoded by the deposited clone, as commonly defined by the structure of its precursor, *i.e.*, "the precursor amino acid sequences," which are processed to mature forms of IL-20 that do not include amino acid residues such as a leader or secretory sequence of the precursor form; and (2) one skilled in the art reading the instant specification would recognize that the inventors had possession of polynucleotides encoding the mature forms of IL-20 encoded by the deposited clone as claimed.

A. The Specification Describes Mature Forms of IL-20

The specification contains a description of the mature forms of IL-20 that would allow one skilled in the art to visualize or recognize the subject matter of the claimed invention, as required by the relevant caselaw. *See, e.g., Enzo Biochem, Inc. v. Gen-Probe Inc.*, 285 F.3d 1013, 1018, 62 U.S.P.Q.2d 1289 (Fed. Cir. 2002) (citing *University of California v. Eli Lilly & Co.*, 119 F.3d 1559, 1568, 43 U.S.P.Q.2d 1398, 1406 (Fed. Cir. 1997)).

In particular, the specification describes mature forms of IL-20 as those forms of IL-20 which are processed and secreted as a result of expression of the defined IL-20 precursor sequences described by structure (*i.e.*, "the precursor amino acid sequences"). The instant specification describes the mature forms of IL-20 as those portions of the preprotein (*i.e.*,"the precursor amino acid sequences") having the leader sequence cleaved by the host cell to form the mature forms of the polypeptide. *See, e.g.*, page 9, line 30 to page 10, line 10. The mature forms of IL-20 protein are described as those portions of the proprotein that remain following cellular processing of the prosequence. *See id.* The mature forms of the IL-20 protein that the polynucleotides of the claims encode are thus expressed and proteolytically processed forms of "the precursor amino acid sequences" such that the resulting mature forms of the polypeptide do not include amino acid residues such as the leader or secretory sequence of the proprotein. *See id.* In particular, the specification states that:

> By the 'mature IL-20 polypeptide having the amino acid sequence encoded by the human cDNA in HTSGS30' is meant the mature form(s) of the IL-20 protein produced by expression in a mammalian cell (e.g., COS cells, as described below) of the complete open reading frame encoded by the human DNA sequence of clone HTSGS30 which was deposited with the ATCC on two separate occasions (*Id.* at page 10, lines 6-10).

The Examiner appears to contend that the specific molecular structure is required in order to fulfill the written description requirement, because one skilled in the art would allegedly not be able to envision the exact amino acid sequence of the polypeptides encoded by the claimed polynucleotides. Applicants respectfully submit that the instant specification describes the molecular structure of the precursor form of IL-20 (including providing SEQ ID NO:2), and the production of mature forms of IL-20 in various mammalian expression host cell systems. *See, e.g.*, page 3, lines 11-13; page 4, lines 10-

13; page 10, lines 6-10; and Example 3 (describing expression in mammalian host cells including "human Hela, 293, H9 and Jurkat cells, mouse NIH3T3 and C127 cells, Cos 1, Cos 7 and CV1, quail QC1-3 cells, mouse L cells and Chinese hamster ovary (CHO) cells." *See, e.g.,* page 53, lines 33-35). Furthermore, the specification characterizes the structure of the mature form of IL-20 so produced; *i.e.*, the specification expressly states that the mature form of IL-20 secreted from a host cell lacks the leader or secretory sequence. *See, e.g.,* page 9, line 30 to page 10, line 10. Thus, given the description of the mature forms of "the precursor amino acid sequences", one skilled in the art would be able to envision the polynucleotides encompassed by the claims, which encode such mature forms of IL-20.

B. The Specification Conveys To One Skilled in the Art that Applicants Were in Possession of the Claimed Invention

One of ordinary skill in the art would not only be able to visualize or recognize the identity of the subject matter of the claimed invention, but would recognize that Applicants were in possession of the claimed invention. Applicants respectfully submit that the response to the previously filed Office Action, dated September 14, 2001, demonstrates that based on the description in the instant specification, one of ordinary skill in the art would recognize that the inventors were in possession of polynucleotides encoding the mature forms of IL-20 encoded by the deposited clone, as required by the relevant caselaw. *See, e.g., Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555, 1563, 19 U.S.P.Q.2d 1111, 1117 (Fed. Cir. 1991).

The Examiner contends that since the structure of the mature form may vary depending on the host cell, it is not clear that the applicant was in possession of the

"mature form." Applicants respectfully reassert that contrary to the Examiner's opinion, the mature, processed form is an inherent property of the cellular expression of the precursor form of IL-20 described in the specification. The host cell proteolytic processing of the mature form is an inherent property conferred by the structure of the precursor form of IL-20 – the capacity of the precursor to be processed is a consequence of its native sequence (also described in the specification as SEQ ID NO:2), even if the processing may vary depending on the expression system used. Thus, the capacity of the IL-20 polypeptide to be expressed and proteolytically processed to the mature form of the protein is a natural and intrinsic property of that molecule.

Further, Applicants respectfully submit that courts have consistently held that in order to meet the written description requirement, applicants need not utilize any particular form of disclosure to describe subject matter claimed, but only that the description must clearly allow persons of ordinary skill in the art to recognize that the inventor was in possession of what is claimed. *See, e.g., In re Alton,* 76 F.3d 1168, 1172, 37 U.S.P.Q.2d 1578, 1581 (Fed. Cir. 1996). If a person of ordinary skill in the art would have understood the inventor to have been in possession of the claimed invention at the time of filing, even if every nuance of the claims is not explicitly described in the specification, then the adequate written description requirement is met. *Id.* at 1175, 37 U.S.P.Q.2d at 1583 to 1584. An adequate written description of a claimed invention "requires a precise definition, such as by structure, formula, chemical name, or physical properties, not a mere wish or plan for obtaining the claimed chemical invention." *Eli Lilly*, 119 F.3d at 1566, 43 U.S.P.Q.2d at 1404 (quoting *Fiers v. Revel*, 984 F.2d 1164, 1171, 25 U.S.P.Q.2d 1601, 1606 (Fed. Cir. 1993)). The disclosure must allow one skilled in the art to visualize or recognize the identity of the subject matter of the claimed invention. *See Enzo Biochem,*

285 F.3d 1013 at 1018, 62 U.S.P.Q.2d at 1292 (citing *Eli Lilly*, 119 F.3d at 1568, 43 U.S.P.Q.2d at 1406).

In the instant case, one skilled in the art would recognize that the mature form of IL-20 was indeed in the inventor's possession. Although the specification does not explicitly define the beginning and end of the processed, mature form of the IL-20 polypeptide encoded by the deposited clone by amino acid sequence, the common defining features of the genus of the mature form of IL-20 is adequately described on the basis of its structure, chemical and physical properties, as well as a common method of production to allow one skilled in the art to visualize and recognize the subject matter of the claimed invention. Moreover, the specification provides the proprotein and predicted mature form of SEQ ID NO:2, and specifically discloses both how to predict the cleavage point of the proprotein (page 10, lines 11-19), and how to confirm the amino terminal sequence of such mature forms by microsequencing (page 53, lines 18-20).

C. The Caselaw Cited by the Examiner is Distinguishable from the Facts of the Present Case

In addition, Applicants also take this opportunity to address and explain why the often-cited *Eli Lilly* and *Amgen v. Chugai* cases (as well as the recently decided *Enzo Biochem* case), are of very limited precedential value to the present situation because the facts of each case can be distinguished and are not applicable to the instant factual circumstances.

Eli Lilly involved generic claims to mammalian cDNAs encoding insulin, while the specification disclosed only a single species – the nucleotide sequence for the rat insulin gene. The Federal Circuit found the generic claims lacking in written description because

the specification failed to describe structural features commonly possessed by members of the genus. In other words, the disclosure of the rat cDNA sequence alone did not provide enough information to claim the other unknown mammalian sequences. Thus, the court found that the written description requirement was not satisfied for generic claims directed to all mammalian insulin cDNAs, which were unknown, when only one species is disclosed in the specification. *Id.* at 1565, 43 U.S.P.Q.2d at 1403.

Similarly, *Enzo Biochem* involved claims to nucleic acid probes that hybridize to a particular bacterial genome. Not only did the specification fail to describe the probes by sequence, the specification also failed to disclose the sequence of the bacterial genome. Thus, even further removed from *Eli Lilly, Enzo Biochem* was trying to claim an unknown sequence (*e.g.*, a probe) that was related to another undisclosed sequence (the bacterial genome). The Federal Circuit found the claimed invention lacking in written description. Citing *Eli Lilly*, the Federal Circuit concluded that an adequate written description of genetic material "requires a precise definition, such as by structure, formula, chemical name, or physical properties."

In *Amgen*, Chugai contended that Fritsch was a prior inventor of claims to the EPO gene because he conceived of a generalized approach for screening a DNA library that might be used to identify and clone the human EPO gene of then unknown constitution. The court found that such a conception of an approach that might result in cloning the gene was speculative and clearly not conception of a purified and isolated DNA sequence encoding the gene. The court held that in order for the conception of a process to satisfy the conception of an unknown composition of matter, such as a gene, the process had to be sufficiently specific that one skilled in the relevant art would succeed in cloning the gene. Indeed, expert testimony provided that success in cloning the human EPO gene using the

approach set forth in the specification was not assured until the gene was in fact isolated and its sequence known. Thus, the court held that conception of a general process of cloning did not provide conception of an unknown gene. Instead, conception of a gene requires that the inventor have "a mental picture of the structure of the chemical *or is able to define it by its method of preparation, its physical or chemical properties, or whatever characteristics sufficiently distinguish it.*" *Amgen*, 927 F2d at 1206, 18 U.S.P.Q.2d at 1021 (emphasis added).

It is important to recognize that in *Amgen,* Fritsch knew neither the structure nor physical characteristics of the claimed EPO gene and furthermore had only a speculative method for obtaining the claimed subject matter. The court's holding that adequate conception of the DNA sequence was contingent upon reduction to practice was based on the uncertainties of the method of obtaining the unknown sequence. In contrast, Applicants submit that the instant claimed subject matter has been characterized and defined not only by a method of preparation, but by physical properties (*e.g.* amino acid sequence of the precursor) and biological activity as set forth *supra.* Further, Applicants submit that as described by the instant specification, the processing of the defined precursor to its mature form is neither a speculative nor prophetic method of obtaining the instant claimed subject matter.

Unlike *Amgen, Eli Lilly* or *Enzo Biochem*, the instant claimed subject matter is not unknown. Instead, in the present case the claimed subject matter is defined by the structure of its precursor, (i.e., by its amino acid and nucleic acid sequence) which is processed to biologically active mature forms that do not contain the leader or secretory sequence of the precursor form. Such disclosure would allow one skilled in the art to visualize or recognize the identity of the subject matter of the claim, as discussed *supra.*

Moreover, Applicants invite the Examiners' attention to *In re Edwards*, 568 F.2d 1349, 196 U.S.P.Q. 465 (CCPA 1978), where the court specifically held under factual circumstances similar to the instant circumstances, that describing the claimed invention as a process of making it is sufficient to meet the written description requirement for a compound claim. In particular, the court in *Edwards* held that the primary concern is whether the description requirement has been complied with, not the mode selected for compliance. In *Edwards* the claimed compound was the predominant product of two specifically defined reactions. The description of the two reactions which resulted in the claimed compound were found to be an adequate written description of the compound because one skilled in the art would be reasonably led to the described reactions and thus, to the claimed compound.

As in *Edwards*, courts have recognized that the primary function of the written description requirement is to insure that an inventor had possession of the claimed subject matter and to allow one skilled in the art to recognize what is claimed. *See In re Blaser*, 556 F.2d 534, 194 U.S.P.Q. 122 (CCPA 1977), *Enzo Biochem*, 285 F.3d 1013, 62 U.S.P.Q. 2d 1289. The written description requirement is satisfied by the disclosure of the claimed subject matter in such a descriptive means, *e.g.*, words, structures, figures and diagrams, to allow one skilled in the art to visualize or recognize the claimed subject matter. *Enzo Biochem*, 285 F.3d 1013.

The Federal Circuit has also noted that the priority application need not use the identical words to describe the claimed invention, if it shows the subject matter claimed with an adequate direction as to how to obtain it. *See Kennecott Corp. v. Kyocera Int'l, Inc.*, 835 F.2d 1419, 1422, 5 U.S.P.Q.2d 1194, 1197 (Fed. Cir. 1987), *cert denied*, 486 U.S. 1008 (1988). It is equally well established that satisfaction of the written description

requirement does not require *in haec verba* antecedence in the originally filed application. *See In re Lukach*, 440 F.2d 1263, 169 U.S.P.Q. 795 (CCPA 1971). The written description requirement can be satisfied by showing that the disclosed subject matter, when given its "necessary and only reasonable construction," inherently (*i.e.*, necessarily) satisfies the limitation in question. *Staehelin v. Secher,* 24 U.S.P.Q.2d, 1513, 1520 (Bd. Pat. Int'f. 1992) ("a specification need not describe the exact details for preparing every species within the genus described"). In general, precedent establishes that although the applicant "does not have to describe exactly the subject matter claimed, the description must clearly allow persons of skill in the art to recognize that [the applicant] invented what is claimed." *In re Gosteli,* 872 F.2d 1008,1012, 10 U.S.P.Q.2d 1614, 1618 (Fed. Cir. 1989).

Given the instant factual circumstances, there can be no doubt that inventors had possession of the claimed invention, as mature forms of a specifically defined precursor are naturally and intrinsically (and not just potentially) generated by their host cells in the manner of the examples provided in the instant specification. The method for obtaining and isolating such mature forms is described in the specification. As evidenced by the description provided in the instant specification, the method provides more than a reasonable expectation that such mature forms can be obtained. The mature forms encoded by the claimed polynucleotides are obtained as a matter of fact in carrying out the steps of the process disclosed in the specification. Accordingly, an adequate description of a mature form as it is obtained from a host cell is, concomitantly, an adequate description of the claimed polynucleotides encoding such mature forms.

In sum, one of ordinary skill in the art would recognize that the Applicants were in possession of the claimed invention, *i.e.*, polynucleotides encoding mature forms of the

precursor amino acid sequences of IL-20. In view of the teachings of the specification, there can be no question that the claimed invention has been adequately described to allow one skilled in the art to visualize and recognize that which is claimed. Further, it is unnecessary for the specification to explicitly define by amino acid sequence, the beginning and end of the processed, mature form of IL-20 in order for one skilled in the art to recognize and identify a mature form that is naturally and inherently produced when expressed by a host cell.

Thus, the instant specification contains sufficient information to allow one of ordinary skill in the art to recognize that Applicants have satisfied the written description requirements. Hence, the rejection under 35 U.S.C. §112, first paragraph, should be withdrawn.

Conclusion

In view of the foregoing remarks, applicants believe that the Examiner's rejection under 35 U.S.C. § 112, first paragraph, has been overcome and this application is now in condition for allowance. An early notice to that effect is urged. The Examiner is invited to call the undersigned at the phone number provided below if any further action by applicant would expedite the examination of this application.

Finally, if there are any fees due in connection with the filing of this paper, please charge the fees to our Deposit Account No. 08-3425. If a fee is required for an extension

of time under 37 C.F.R. § 1.136 not accounted for above, such an extension is requested and the fee should also be charged to our Deposit Account.

Respectfully submitted,

Dated: June 3, 2002

Mark J. Hyman (Reg. No. 46,789)
Attorney for Applicants

Human Genome Sciences, Inc.
9410 Key West Avenue
Rockville, MD 20850
Telephone: (240) 314-1224

Enclosures
MMW/MJH/CEW/mm